Claims

1. A method for analyzing a polymer comprising:

providing the polymer having first and second unit specific markers, the first unit specific marker including a first label and the second unit specific marker including a second label, wherein the first and second unit specific markers are spaced apart on the polymer by a separation distance;

providing a detection zone adapted to detect emission signals, the detection zone characterized by a zone distance;

establishing a timing event;

moving the polymer through the detection zone at a velocity;

detecting a first emission signal emitted by the label of the first unit specific marker as the first unit specific marker passes through the detection zone;

detecting a second emission signal emitted by the label of the second unit specific marker as the second unit specific marker passes through the detection zone;

calculating a proportion of the first emission signal and calculating a proportion of the second emission signal that are each detected on a side of the timing event; and

determining the separation distance by comparing the proportion of the first signal and the proportion of the second signal to determine the separation distance in analyzing the polymer.

2. The method of claim 1, wherein calculating the proportion of the first emission signal comprises dividing a first portion of the first signal that is detected before the timing event by all of the first signal.

3. The method of claim 2, wherein calculating the proportion of the second emission signal comprises dividing a first portion of the second signal that is detected before the timing event by all of the second signal

4. The method of claim 1, wherein calculating the proportion of the first emission signal comprises dividing a second portion of the first signal that is detected after the timing event by all of the first signal.

5. The method of claim 4, wherein calculating the proportion of the second emission signal comprises dividing a second portion of the second signal that is detected after the timing event by all of the second signal

6. The method of any of claims 1-5, wherein the first label and the second label are distinct types of labels.

7. The method of claim 6, wherein the timing event comprises a single timing event for calculating the proportion of the first emission signal and calculating the proportion of the second emission signal.

8. The method of claim 7, wherein determining the separation distance comprises multiplying the proportion of the first signal and the proportion of the second signal by the zone distance to define a first distance and a second distance, respectively; and then

subtracting the second distance from the first distance to define the separation distance.

9. The method of claim 7, wherein determining the separation distance comprises subtracting the proportion of the second signal from the proportion of the first signal to define a separation factor; and then

multiplying the separation factor by the zone distance to define the separation distance.

10. The method of any of claims 1-6, wherein the timing event comprises two distinct timing events, a first timing event for calculating the proportion of the first emission signal and a second timing event that occurs one reset time immediately after the first timing event, the second timing event for calculating the proportion of the second emission signal.

11. The method of claim 10, further comprising:

calculating a reset distance by multiplying the velocity by the reset time;

wherein determining the separation distance comprises multiplying the proportion of the first signal and the proportion of the second signal by the zone distance to define a first distance and a second distance, respectively; then

subtracting the second distance from the first distance; and then

adding the reset distance to the first distance to define the separation distance.

12. The method of claim 10, further comprising:

calculating a reset distance by multiplying the velocity by the reset time;

wherein determining the separation distance comprises subtracting the proportion of the second signal from the proportion of the first signal to define a separation factor; then

multiplying the separation factor by the zone distance; and then

adding the reset distance to define the separation distance.

13. The method of any of claims 1-5, wherein the timing event comprises two distinct timing events, a first timing event for calculating the proportion of the first emission signal and a second timing event that occurs later and is separated by one or more timing events within a series of timing events, the second timing event for calculating the proportion of the second emission signal.

14. The method of claim 13, further comprising:

calculating a reset distance by multiplying the velocity by the reset time;

wherein determining the separation distance comprises multiplying the proportion of the first signal and the proportion of the second signal by the zone distance to define a first distance and a second distance, respectively; and

further wherein the second distance is subtracted from the first distance and a number of reset distances equivalent to the number of timing events, are added to the first distance to define the separation distance.

15. The method of claim 13, further comprising:

calculating a reset distance by multiplying the velocity by the reset time;

wherein determining the separation distance comprises subtracting the proportion of the second signal from the proportion of the first signal; and

further wherein the separation factor is multiplied by the zone distance and a number of reset distances, equivalent to the number of timing events, are added to define the separation distance.

16. The method of any of claims 13-15, wherein the first label and the second label comprise similar types of labels.

17. The method of any of claims 13-15, wherein the first label and the second label are distinct types of labels.

18. The method of any of claims 1 -17, wherein the first unit specific marker is different from the second unit specific marker.

19. The method of any of claims 1-18, wherein the first unit specific marker is identical to the second unit specific marker.

20. The method of any of claims 1-19, wherein the polymer is labeled with a third unit specific marker comprising a third label.

21. The method of any of claims 1-20, wherein the first and second unit specific markers are nucleic acid molecules.

22. The method of any of claims 1-21, wherein the first and second unit specific markers are peptide nucleic acid molecules or locked nucleic acid molecules.

23. The method of any of claims 21-22, wherein the first and second unit specific markers have an identical nucleotide sequence.

24. The method of any of claims 21-23, wherein the first and second unit specific markers are less than 12 bases in length.

25. The method of any of claims 21-24, wherein the first and second unit specific markers are at least 4 bases in length.

26. The method of any of claims 1-25, wherein the first label and second label are selected from the group consisting of an electron spin resonance molecule, a fluorescent molecule, a chemiluminescent molecule, a radioisotope, an enzyme substrate, an enzyme, a biotin molecule, an avidin molecule, an electrical charge transferring molecule, a semiconductor nanocrystal, a semiconductor nanoparticle, a colloid gold nanocrystal, a ligand, a microbead, a magnetic bead, a paramagnetic molecule, a quantum dot, a chromogenic substrate, an affinity molecule, a protein, a peptide, a nucleic acid, a carbohydrate, a hapten, an antigen, an antibody, an antibody fragment, and a lipid.

27. The method of any of claims 1-26, wherein the signals are detected using a detection system selected from the group consisting of an electron spin resonance (ESR) detection system, a charge coupled device (CCD) detection system, a fluorescent detection system, an electrical detection system, an electromagnetic detection system, a photographic film detection system, a chemiluminescent detection system, an enzyme detection system, an atomic force microscopy (AFM) detection system, a scanning tunneling microscopy (STM) detection system, an optical detection system, a nuclear magnetic resonance (NMR) detection system, a near field detection system, and a total internal reflection (TIR) detection system.

28. The method of any of claims 1-27, wherein the polymer is a nucleic acid molecule.

29. The method of any of claims 1-28, wherein the polymer is genomic DNA or RNA.

30. The method of any of claims 1-29, wherein the polymer comprises a backbone that includes a label.

31. The method of any of claims 1-30, wherein the reset time is between 0.01 and 1000 milliseconds.

32. The method of any of claims 1-31, wherein the detection zone is circular and the detection distance is a diameter of the detection zone.

33. A computer-readable medium having computer-readable signals stored thereon that define instructions that, as a result of being executed by a computer, instruct the computer to perform a method of determining a separation distance between a first and a second label on a polymer in a system having a detection zone adapted to detect emission signals, the detection zone characterized by a zone distance and adapted to detect a first emission signal and a second emission signal from the first and second label, respectively, when they pass through the detection zone at a velocity, the method comprising acts of:

establishing a timing event;

calculating a proportion of the first emission signal and calculating a proportion of the second emission signal that are each detected on a side of the timing event;

determining the separation distance by comparing the proportion of the first signal and the proportion of the second signal to determine the separation distance.

34. The computer-readable medium of claim 33, wherein calculating the proportion of the first emission signal comprises dividing a first portion of the first signal that is detected before the timing event by all of the first signal.

35. The computer-readable medium of claim 34, wherein calculating the proportion of the second emission signal comprises dividing a first portion of the second signal that is detected before the timing event by all of the second signal

36. The computer-readable medium of claim 33, wherein calculating the proportion of the first emission signal comprises dividing a second portion of the first signal that is detected after the timing event by all of the first signal.

37. The computer-readable medium of claim 36, wherein calculating the proportion of the second emission signal comprises dividing a second portion of the second signal that is detected after the timing event by all of the second signal

38. The computer-readable medium of any of claims 33-37, wherein the first label and the second label are distinct types of labels.

39. The computer-readable medium of claim 38, wherein the timing event comprises a single timing event for calculating the proportion of the first emission signal and calculating the proportion of the second emission signal.

40. The computer-readable medium of claim 39, wherein determining the separation distance comprises multiplying the proportion of the first signal and the proportion of the second signal by the zone distance to define a first distance and a second distance, respectively; and then

subtracting the second distance from the first distance to define the separation distance.

41. The computer-readable medium of claim 39, wherein determining the separation distance comprises subtracting the proportion of the second signal from the proportion of the first signal to define a separation factor; and then

multiplying the separation factor by the zone distance to define the separation distance.

42. The computer-readable medium of any of claims 33-38, wherein the timing event comprises two distinct timing events, a first timing event for calculating the proportion of the first emission signal and a second timing event that occurs one reset time immediately after the first timing event, the second timing event for calculating the proportion of the second emission signal.

43. The computer-readable medium of claim 42, further comprising:

calculating a reset distance by multiplying the velocity by the reset time;

wherein determining the separation distance comprises multiplying the proportion of the first signal and the proportion of the second signal by the zone distance to define a first distance and a second distance, respectively; then

subtracting the second distance from the first distance; and then

adding the reset distance to the first distance to define the separation distance.

44. The computer-readable medium of claim 42, further comprising:

calculating a reset distance by multiplying the velocity by the reset time;

wherein determining the separation distance comprises subtracting the proportion of the second signal from the proportion of the first signal to define a separation factor; then

multiplying the separation factor by the zone distance; and then

adding the reset distance to define the separation distance.

45. The computer-readable medium of any of claims 33-37, wherein the timing event comprises two distinct timing events, a first timing event for calculating the proportion of the first emission signal and a second timing event that occurs later and is separated by one or more timing events within a series of timing events, the second timing event for calculating the proportion of the second emission signal.

46. The computer-readable medium of claim 45, further comprising:

calculating a reset distance by multiplying the velocity by the reset time;

wherein determining the separation distance comprises multiplying the proportion of the first signal and the proportion of the second signal by the zone distance to define a first distance and a second distance, respectively; and

further wherein the second distance is subtracted from the first distance and a number of reset distances equivalent to the number of timing events, are added to the first distance to define the separation distance.

47. The computer-readable medium of claim 45, further comprising:

calculating a reset distance by multiplying the velocity by the reset time;

wherein determining the separation distance comprises subtracting the proportion of the second signal from the proportion of the first signal; and

further wherein the separation factor is multiplied by the zone distance and a number of reset distances, equivalent to the number of timing events, are added to define the separation distance.

48. The computer-readable medium of any of claims 45-47, wherein the first label and the second label comprise similar types of labels.

49. The computer-readable medium of any of claims 45-47, wherein the first label and the second label are distinct types of labels.

50. The computer-readable medium of any of claims 33-49, wherein the first unit specific marker is different from the second unit specific marker.

51. The computer-readable medium of any of claims 33-50, wherein the first unit specific marker is identical to the second unit specific marker.

52. The computer-readable medium of any of claims 33-51, wherein the polymer is labeled with a third unit specific marker comprising a third label.

53. The computer-readable medium of any of claims 33-52, wherein the first and second unit specific markers are nucleic acid molecules.

54. The computer-readable medium of any of claims 33-53, wherein the first and second unit specific markers are peptide nucleic acid molecules or locked nucleic acid molecules.

55. The computer-readable medium of any of claims 53-54, wherein the first and second unit specific markers have an identical nucleotide sequence.

56. The computer-readable medium of any of claims 53-55, wherein the first and second unit specific markers are less than 12 bases in length.

57. The computer-readable medium of any of claims 53-56, wherein the first and second unit specific markers are at least 4 bases in length.

58. The computer-readable medium of any of claims 33-57, wherein the first label and second label are selected from the group consisting of an electron spin resonance molecule, a fluorescent molecule, a chemiluminescent molecule, a radioisotope, an enzyme substrate, an enzyme, a biotin molecule, an avidin molecule, an electrical charge transferring molecule, a semiconductor nanocrystal, a semiconductor nanoparticle, a colloid gold nanocrystal, a ligand, a microbead, a magnetic bead, a paramagnetic molecule, a quantum dot, a chromogenic substrate, an affinity molecule, a protein, a peptide, a nucleic acid, a carbohydrate, a hapten, an antigen, an antibody, an antibody fragment, and a lipid.

59. The computer-readable medium of any of claims 33-58, wherein the signals are detected using a detection system selected from the group consisting of an electron spin resonance (ESR) detection system, a charge coupled device (CCD) detection system, a fluorescent detection system, an electrical detection system, an electromagnetic detection system, a photographic film detection system, a chemiluminescent detection system, an enzyme detection system, an atomic force microscopy (AFM) detection system, a scanning tunneling microscopy (STM) detection system, an optical detection system, a nuclear magnetic resonance (NMR) detection system, a near field detection system, and a total internal reflection (TIR) detection system.

60. The computer-readable medium of any of claims 33-59, wherein the polymer is a nucleic acid molecule.

61. The computer-readable medium of any of claims 33-60, wherein the polymer is genomic DNA or RNA.

62. The computer-readable medium of any of claims 33-61, wherein the polymer comprises a backbone that includes a label.

63. The computer-readable medium of any of claims 33-62, wherein the reset time is between 0.01 and 1000 milliseconds.

64. The computer-readable medium of any of claims 33-63, wherein the detection zone is circular and the detection distance is a diameter of the detection zone.

65. A method for analyzing a polymer comprising:

a) providing a detection zone having a known detection resolution, the detection zone characterized by a zone distance;

b) labeling the polymer with first and second unit specific markers, the first unit specific marker including a first label and the second unit specific marker including a second label distinct from the first label, wherein the first and second unit specific markers are spaced apart on the polymer by a separation distance such that, if the labels were not distinct from each other, they would be separated by a distance less than the detection resolution;

c) exposing the polymer labeled as in (b) to the detection station to produce distinct first and second signals arising from the first and second labels;

d) establishing a timing event;

e) moving the polymer through the detection zone at a velocity;

f) identifying a first emission signal emitted by the label of the first unit specific marker as the first unit specific marker passes through the detection zone;

g) identifying a second emission signal emitted by the label of the second unit specific marker as the second unit specific marker passes through the detection zone;

h) calculating a proportion of the first emission signal and calculating a proportion of the second emission signal that are each detected on a side of the timing event; and

i) determining the separation distance by comparing the proportion of the first signal and the proportion of the second signal to determine the separation distance in analyzing the polymer.